REMARKS

Applicants appreciate Examiner's indication that claims 7, 8, 10-12, 23-26, 28 and 29 are in condition for allowance. In view of the lengthy prosecution to date, Applicants hereby cancel all rejected claims, claims 1-4, 6, 20-22 and 27, solely to expedite issuance of a patent. Cancellation of claims should not be interpreted as an acquiescence to the outstanding rejections. Applicants reserve the right to pursue similar claims in this or related applications.

Rejection of Claims 1, 3, 4, 20, 22 and 27 Under 35 U.S.C. 102 (b) and 103

The Examiner has rejected claims 1, 3, 4, 20, 22 and 27 as allegedly anticipated under 35 U.S.C. 102(b) by Candrian et al. (Applied and Environmental Microbiology (1991) April, pages 955-961).

The Examiner states, "Candrian et al. teach a primer comprising the following pattern of universal and designate nucleotides which meet the limitations of [claim 1]: 5' **TT**ITTCTGTATTITCTTT**IICIIC**TTTIIITC**AG** 3'. Further, claims 3 and 4 are also anticipated...in that a plurality of instances of the pattern exists and designate nucleotides are bound to the end of the sequence."

The Examiner applies similar arguments to claims 20, 22 and 27.

The Examiner further rejects claims 1-4, 6, 20-22 and 27 under 35 U.S.C. 103(a) as being unpatentable over Candrian et al. in view of Bergstrom et al. (Nucleic Acid Research (1997) Vol. 25, pages 1935-1942).

The Examiner argues, "Candrian et al. teach the use of inosine-containing oligonucleotide primers for enzymatic amplification of different alleles...Candrian et al. do not teach the use of 5-nitroindole or 3-nitropyrrole nucleotide analogs. However, Bergstrom et al. do teach incorporation of these analogs into oligonucleotides. It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to utilize 5-nitroindole and 3-nitropyrrole in the primers designed by Candrian et al."

Applicants respectfully assert that Candrian et al. does not anticipate any of the claims of the present application. It is axiomatic that in order to anticipate a claim, a reference must disclose each and every element of the claimed subject matter, either explicitly or inherently. Here, all of the pending claims, including claims 1, 3, 4, 20, 22 and 27 contain a "universal" nucleotide or nucleotide analog. As understood in the specification and in the now-extensive prosecution record, the term "universal" refers to: "an entity (or collection of entities mutually substituted at a position) that is relatively non-specific with respect to all of A, T, C and G. Exemplary universal bases are 5-nitroindole and 3-nitropyrrole. As would be appreciated by one of skill in the art, any 'universal' base will have some heterogeneity in free energy of hybridization with different partners." (see Applicants' response dated Aug. 3, 2001).

Applicants submit that inosine is not a "universal" nucleotide. Inosine is known in the art to hybridize specifically with A and C but not with G or T. For example, see Macevicz et al. (WO 90/04652, previously cited in this prosecution) at page 4, line 16, which reads, "because deoxyinosine (I) forms nearly equally strong base pairs with A and C, but forms only a weak or destabilizing base pair with either G or T, deoxyinosine can replace G and T in a probe." Accordingly, inosine cannot be considered to be a universal nucleotide as the term is used in this application. However, Applicants note that a degenerate position created by the use of a mixture of I, C and A at a single position in a probe would be equivalent to a universal nucleotide. Such a mixture is not suggested by Candrian et al.

Accordingly, Candrian et al. does not teach or suggest, explicitly or implicitly, the use of a probe containing a "universal" nucleotide and cannot, therefore, anticipate the present claims.

Furthermore, Applicants assert that there would have been no motivation to replace inosine in the probes of Candrian et al. with the universal nucleotides described in Bergstrom et al. Candrian et al. achieved sufficient degeneracy for their intended purpose (DNA amplification) by using inosine and would not have been motivated to seek nucleotides having greater degeneracy.

For these reasons, Applicants maintain that all of the present claims are novel and non-obvious with respect to Candrian et al. and with respect to Candrian et al. in view of Bergstrom et al.

Nonetheless, solely to expedite prosecution, all presently rejected claims are canceled, without prejudice. Therefore claims 1-4, 6, 20-22 and 27 are canceled, rendering all rejections moot.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Applicants hereby request that any fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945.**

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Respectfully submitted,

By _____

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